

Regional Clinical Advice Response Service 14/05/21

For any COVID-19 vaccination related queries or to escalate an incident please contact:
england.swcovid19-cars@nhs.net

Please note that going forward and in line with the RVOC and NVOC, RCARS will now operate between the hours of 8am and 6pm over the weekend.

**PLEASE SHARE WITH ALL RELEVANT STAFF INVOLVED WITH THE
VACCINATION PROGRAMME**

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JCVI Advises On COVID-19 Vaccine for People Aged Under 40

The Joint Committee on Vaccination and Immunisation (JCVI) has issued advice to the UK government on the use of the coronavirus (COVID-19) Oxford/AstraZeneca vaccine for people aged under 40.

The committee has reviewed the latest available evidence, including the current COVID-19 infection rate, the scale and pace of the vaccine programme and modelling of the timing and size of any third pandemic wave.

This has been considered alongside the latest advice from the Medicines and Healthcare products Regulatory Agency (MHRA) on extremely rare cases of concurrent thrombosis (blood clots) and thrombocytopenia (low platelet count) following the first dose of the Oxford/AstraZeneca vaccine.



The chances of a younger person becoming seriously ill with COVID-19 get smaller as infection rates increasingly come under control in the UK.

Considering this alongside the portfolio of vaccines available in the UK in the coming months and taking a precautionary approach in relation to the extremely small risk of thrombosis and thrombocytopenia following the first dose of the Oxford/AstraZeneca vaccine, the JCVI has

advised a preference for adults aged 30 to 39 without underlying health conditions to receive an alternative to the Oxford/AstraZeneca vaccine – where available and only if this does not cause substantial delays in being vaccinated.

For more information, please see [JCVI advises on COVID-19 vaccine for people aged under 40 - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/news/jcvi-advises-on-covid-19-vaccine-for-people-aged-under-40)

Update on National Incident In Response To Reports Of Thrombosis With Thrombocytopenia Following Vaccination With The COVID-19 Astrazeneca Vaccine – National Infection Service Briefing

Please read attached full briefing with references which is summarised below:

Background and Interpretation:

This briefing note is an update to the briefing note issued on the 19th April 2021 relating to the national incident response to reports of thrombosis with thrombocytopenia following the AstraZeneca (AZ) COVID-19 vaccine. Since the 4th January to 28th April 2021, 22.6 million first doses and 5.9 million second doses of the AZ vaccine have been administered across the UK (1). The COVID-19 vaccine programme in England has been estimated to have prevented 10,400 deaths in adults aged 60 years and older till the end of March (2) with a vaccine effectiveness of a single dose against hospitalisation estimated at 80% for both the Pfizer/BioNTech and the AZ vaccines (3).

Based on reporting through the MHRA Yellow Card Scheme, as of 28th April 2021, there have been 242 suspected cases of thromboembolic events occurring with thrombocytopenia across the UK following AZ vaccination, giving an overall incidence of 10.5 cases per million first doses (1). To date, no confirmed cases have occurred after the second dose of AZ vaccine. Of the suspected cases, 93 reports are of a very rare and specific type of syndrome of blood clots in the cerebral veins, known as cerebral venous sinus thromboses (CVST) occurring together with low platelet counts. This syndrome has affected patients of all ages and genders, although there does appear to be a trend towards an increased incidence in younger adult age groups. The cases are unusual because despite thrombocytopenia, there is progressive thrombosis, primarily venous, including CVST and portal vein thrombosis, as well as the more usual presentations of deep vein thrombosis and pulmonary embolism. Arterial events have also been reported. Antibodies to platelet factor 4 (PF4) have been identified and so this syndrome appears to have similarities to heparin-induced thrombocytopenia (HIT), but in the absence of patient exposure to heparin treatment. Early recognition and appropriate treatment with Intravenous Immunoglobulin (IVIG) and the avoidance of platelet transfusions appear to improve outcomes, with current case fatality rates estimated at 20%. PHE Briefing Note 2021/29 Issued 07/05/21

Investigations are underway to understand the biological mechanisms and whether this is related to the vaccine platform (the way in which the vaccine delivers antigen) or some other immunological mechanism. There has been a small number of reports of a similar syndrome

following receipt of the Johnson&Johnson /Janssen COVID-19 vaccine (another adenovirus vector vaccine) in the USA. Following a detailed investigation and temporary pause in the use of the vaccine in the USA, the CDC and FDA announced the resumption of the use of the Johnson&Johnson /Janssen vaccine on 23rd April 2021. This vaccine is not currently approved for use in the UK. There is currently no evidence to suggest these rare events have occurred in the UK following administration of either the Pfizer/BioNTech or Moderna COVID-19 vaccines.

Updated Advice issued by UK Joint Committee on Vaccination and Immunisation (JCVI) on Use of AZ Vaccine

The Joint Committee on Vaccination and Immunisation (JCVI) has carefully assessed the overall risk benefit of the use of the AZ vaccine in the UK population. After considering the relative balance of benefits (in terms of deaths, ICU and hospital admissions averted) and risks (based on reported adverse events through the Yellow Card Scheme), on 7 April 2021, JCVI advised that, for adults aged <30 years without underlying health conditions that put them at higher risk of severe COVID-19 disease, there should be a preference for an alternative to the AZ COVID-19 vaccine, if available.

JCVI has continued to review the available data on the current epidemiology, benefit-risk profile by age, modelling predictions on future disease trends and the current forecast on vaccine supply. Given the risk (albeit extremely rare) of these adverse events associated with the AZ vaccine, the current control of COVID-19 in the UK, model predictions of the potential scale and timing of a future wave, and promising forecasts for the availability of vaccines in the UK, on 7th May, the JCVI has issued the following [updated advice](#):

- In addition to those aged under 30, unvaccinated adults aged 30 - 39 years who are not in a clinical priority group at higher risk of severe COVID-19 disease, should be preferentially offered an alternative to the AZ vaccine, where possible and only where no substantial delay or barrier in access to vaccination would arise.
- For those aged 18-29 years the precautionary advice for a vaccine preference is stronger, reflecting a gradient in the benefit-risk balance with age.
- For adults aged 40 years and above and those below 40 years with underlying clinical conditions, the overall risk benefit assessment remains in favour of continuing use of the AZ vaccine.

This advice is specific to the current UK context and is based on the prevailing favourable epidemiology of disease, availability of alternatives to the Astra-Zeneca vaccine, and strength of the vaccine programme.

Those who have received their first dose of AZ vaccine without suffering this rare side-effect, should continue to be offered the second dose to complete the course.

Cautions and contraindications for use of AZ Vaccine

Currently there have not been any underlying risk factors that have been identified. There is no evidence to indicate that individuals with a prior history of thrombosis or known risk factors for thrombosis (including those on the oral contraceptive pill) are at increased risk of developing this immunological reaction following vaccination with the AZ vaccine. Furthermore, for the majority of individuals, the risk of recurrent thrombosis due to COVID-19 infection is far greater than the risk of this syndrome. More than a fifth of hospitalised patients with COVID-19 have evidence of blood clots, and the presence of these almost doubles the risk of death. A revision

to the COVID-19 [Green book chapter](#) is available with updated information on cautions and contraindications for the AZ vaccine.

There have not been any confirmed cases of this syndrome in pregnant women to date, and prothrombotic states such as pregnancy and contraception are not likely to confer a higher risk. However, because of more extensive experience and use of the Pfizer and Moderna vaccines in pregnant women in the USA, these vaccines are preferred in pregnancy.

Case Reporting

It is very important that all suspected cases are reported to both the MHRA on the [COVID-19 Yellow Card scheme](#) and to PHE's clinical reporting scheme at https://cutt.ly/haem_AE. The PHE clinical reporting scheme collects patient identifiable information with details of the clinical presentation, dates of vaccination, vaccine product received and any underlying conditions. In order to minimise burden on reporters, for cases reported on the PHE clinical reporting scheme first, the last page of the survey allows all the inputted answers to be copied, and relevant information can then be directly pasted into the COVID-19 Yellow Card form.

Clinical Investigation and Management

It is important to ensure all health professionals are alert to relevant symptoms which require further clinical review and investigation. It is recommended that an urgent full blood count be considered in any patient presenting more than 4 days and within 28 days of coronavirus vaccination with:

- New onset of severe headache, which is getting worse and does not respond to simple painkillers
- An unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- New onset of unexplained pinprick bruising or bleeding
- Shortness of breath, chest pain, leg swelling or persistent abdominal pain

Patients should be urgently referred to hospital and to appropriate specialist services for further assessment, particularly if the symptoms are unexplained and present in combination with thrombocytopenia. Further guidance for secondary care are available [here](#) with specific guidance produced for [Emergency Departments and Acute Medical Units and primary care](#).

The [Green Book](#) has been updated and a range of resources for the public and health professionals have been made available. These resources will continue to be updated as new information becomes available, so we recommend linking to the collection to ensure that you are providing the most up-to-date guidance: [COVID-19 vaccination and blood clotting - GOV.UK \(www.gov.uk\)](#)

Implications and recommendations for PHE Regions

PHE Regions are asked to note the updated advice on the use of the AZ vaccine and guidance available for primary and secondary care. PHE Regions are requested to cascade this briefing note to local primary and secondary care services to ensure colleagues are aware of the available guidance and how to report suspected cases. PHE Briefing Note 2021/29 Issued 07/05/21

Implications and recommendations for PHE sites and services

PHE sites and services are asked to note the updated advice on the use of the AZ vaccine and guidance for reporting, investigating and managing suspected cases.

Implications and recommendations for PHE Screening and Immunisation teams

An increase in calls requesting advice are expected. Screening and immunisation teams are requested to note the updated information and guidance. SITs are requested to cascade this briefing note to their local primary care teams.

Implications and recommendations for local authorities

Local Authorities are asked to note the updated advice on the use of the AZ vaccine and guidance for primary and secondary care.

Recommendations for NHS trusts and COVID-19 immunisation services

Services are asked to ensure that anyone being offered an AZ COVID-19 vaccination is given the [COVID-19 vaccination and blood clotting guide](#) before vaccination. All people receiving any COVID-19 vaccine should be given the patient vaccination leaflet 'What to expect after vaccination' and know to seek appropriate healthcare assistance if required. These resources have been updated to reflect that latest guidance. All leaflets are available to order as paper copies and in other accessible formats including translations. Primary care services should be aware of these symptoms and refer to secondary care as appropriate following assessment.

Use of the AstraZeneca COVID-19 (AZD1222) Vaccine: Updated JCVI Statement, 7 May 2021 – Full Statement

The full statement can be read [here](#).

Introduction

Since the start of the pandemic over 4.4 million COVID-19 infections have been confirmed in the UK causing more than 127,000 deaths. Over 34 million people have now received their first dose of COVID-19 vaccine, which Public Health England (PHE) estimates has prevented at least 10,000 deaths. Analysis of post-marketing surveillance data in the UK demonstrates that vaccination is highly effective and substantially reduces the risk of infection and severe COVID-19 disease and reduces onward transmission.

There have been reports of extremely rare adverse events of concurrent thrombosis (blood clots) and thrombocytopenia (low platelet count) following vaccination with the first dose of AstraZeneca ChAdOx1 nCoV-19 vaccine (AZD1222). There have been no safety concerns identified for thrombosis/thrombocytopenia associated with the second dose of the AstraZeneca (AZD1222) vaccine, nor with other COVID-19 vaccines currently approved for use in the UK (Pfizer-BioNTech and Moderna).

On 7 April 2021, after considering the relative balance of benefits and risks, the Joint Committee on Vaccination and Immunisation (JCVI) advised that, for adults aged under 30 years without underlying health conditions that put them at higher risk of severe COVID-19

disease, there should be a preference for an alternative to the AstraZeneca (AZD1222) vaccine, if available.

Current situation in the UK

The Medicines and Healthcare products Regulatory Agency (MHRA) has continued to review cases of these extremely rare adverse events, including those reported retrospectively, and data on the frequency of these events by age is now more precise. The latest reports on this adverse event are available from the MHRA's [coronavirus vaccine – weekly summary of Yellow Card reporting](#).

The available data suggests there is a slightly higher incidence (number of cases per million doses of vaccine given) reported in the younger compared to older adult age groups. There are currently no known risk factors for this extremely rare condition, which appears to be an idiosyncratic reaction on first exposure to the AstraZeneca (AZD1222) vaccine.

Consequent on lockdown measures and the ongoing successful deployment of the COVID-19 mass vaccination programme, COVID-19 incidence is currently low, as are COVID-19 associated hospitalisations and deaths. A number of mathematical models have been reviewed on the potential impact of any resurgence of COVID-19 in the UK. These models indicate that as COVID-19 restrictions are lifted across the country, the number of cases is likely to rapidly increase sometime in the second half of 2021. As such, the current high levels of vaccine uptake and high pace of vaccine deployment are critical to maintaining control over COVID-19 in the UK, especially as physical distancing measures are progressively relaxed. Strong and rapid vaccine coverage will help to minimise the health, social and economic impact of any future wave of COVID-19.

The vaccine supply situation for phase 2 of the programme has been carefully examined. Current forecasts indicate that it will be possible to complete phase 2 by offering the Pfizer-BioNTech or Moderna vaccines for individuals under 40 years of age who are yet to receive their first dose, without materially impacting on timelines for delivery of phase 2. However, vaccine supply forecasts are not completely certain, and it should be recognised that these could change at any time.

Updated advice

JCVI's advice is based on the available data on the current epidemiology, benefit-risk profile by age, modelling predictions on future disease trends and the current forecast on vaccine supply. Given the risk (albeit extremely rare) of these adverse events associated with the AstraZeneca (AZD1222) vaccine, the current control of COVID-19 in the UK, model predictions of the potential scale and timing of a future wave, and promising forecasts for the availability of vaccines in the UK, JCVI agreed its advice should be updated.

JCVI advises that, in addition to those aged under 30, unvaccinated adults aged 30 to 39 years who are not in a clinical priority group at higher risk of severe COVID-19 disease, should be preferentially offered an alternative to the AstraZeneca COVID-19 (AZD1222) vaccine, where possible and only where no substantial delay or barrier in access to vaccination would arise.

For those under 40 years who are of older age, male, obese (BMI above 30), from certain ethnic minority backgrounds or experiencing socio-economic deprivation, the risks of acquiring

and/or suffering complications of COVID-19 are higher. Every effort should be made to remove barriers to accessing vaccination in those individuals.

For those aged 18 to 29 years the precautionary advice for a vaccine preference is stronger, reflecting a gradient in the benefit-risk balance with age.

This new advice is specific to the current UK context and is based on all of the following remaining favourable:

- the current low incidence of disease
- the availability of alternatives to the Astra-Zeneca (AZD1222) vaccine
- the strength of the whole vaccine programme in terms of maintaining speed and uptake

Should there be a deterioration in any of the above factors, JCVI advises that vaccination of adults aged 30 to 39 years with any of the UK-authorized vaccines is always better than no vaccination, except where there are specific contraindications.

Due to its storage and transport requirements, the AstraZeneca (AZD1222) vaccine is much more easily delivered in some settings, and in these settings may be the only vaccine it is practical to offer. In such circumstances JCVI advises that the benefits of receiving the AstraZeneca (AZD1222) vaccine outweigh the risks, and individuals in this event should be offered the AstraZeneca (AZD1222) vaccine.

JCVI considers that there continues to be no safety concerns for this extremely rare adverse event following receipt of a second dose of AstraZeneca (AZD1222) vaccine. All those who have received a first dose of the AstraZeneca (AZD1222) vaccine should continue to be offered a second dose of AstraZeneca (AZD1222) vaccine, irrespective of age. The second dose will be important for longer lasting protection against COVID-19.

JCVI advises that all individuals offered a COVID-19 vaccine should be fully informed about the benefits and risks of vaccination and consent accordingly. This should include:

- clear information on the extremely rare thrombosis/thrombocytopenia adverse events
- how to monitor for symptoms that might be related to the adverse event
- what action should be taken by individuals and health professionals in the event of such symptoms arising

PHE is preparing updated information for those being offered COVID-19 vaccines, and for health professionals, which will be available through the GOV.UK website.

Updated Publication – Covid-19 Vaccination: Information for Healthcare Practitioners

This publication was updated on 11th May to include important new guidance the exceptional circumstances in which a different second vaccine to the first can be given:

Interchangeability of different COVID-19 vaccines There is no evidence as to the interchangeability of the different COVID-19 vaccines although studies are underway. Therefore, every effort should be made to determine which vaccine the individual received for their first dose and to complete the 2-dose course with the same vaccine. For individuals who started the schedule and who attend for vaccination at a site where the same vaccine is not available, for example, if the individual received their first dose abroad, or where the

first product received is unknown, it is reasonable, in these COVID-19 vaccination programme: Information for healthcare practitioners 13 circumstances, to offer 1 dose of the locally available product to complete the schedule (see Appendix 1 and Individuals who received COVID vaccination overseas section below). This option is preferred if that individual is likely to be at immediate high risk or is considered unlikely to attend again. In these circumstances, as all 3 of the COVID-19 vaccines currently authorised in the UK are based on the spike protein of the virus, it is likely that the second dose will help to boost the response to the first dose. Further doses of vaccine are not required unless additional information becomes available.

See link below:

[COVID-19 vaccination: information for healthcare practitioners - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/covid-19-vaccination-information-for-healthcare-professionals)

Updated Publication – COVID-19: The Green Book, Chapter 14a

7 May 2021: Updated to include additional information on the eligibility and safety of the AstraZeneca vaccine.

The Green Book Chapter 14a can be accessed [here](#).

Updated Guidance: Information for Healthcare Professionals on Blood Clotting Following COVID-19 Vaccination

Updated 7 May 2021

The full guidance can be read at the link below:

[COVID-19 vaccination: blood clotting information for healthcare professionals - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/publications/covid-19-vaccination-blood-clotting-information-for-healthcare-professionals)

Updated Guidance: COVID-19 Vaccination and Blood Clotting Guide – for Anyone Being Offered the AstraZeneca Vaccination

The updated leaflet can be accessed at the below link:

<https://www.gov.uk/government/publications/covid-19-vaccination-and-blood-clotting>

Copies can be ordered now using the product code: [COV2020700V2](#). This will go into production on Monday and will be dispatched from Wednesday 12th May. We recommend photocopying required stock in the interim.

All COVID-19 vaccination queries and incidents should be directed to:
england.swcovid19-cars@nhs.net